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National Estimates of Insulin-related Hypoglycemia and Errors Leading to Emergency Department Visits and Hospitalizations

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Abstract

Importance—Detailed, nationally-representative data describing high-risk populations and circumstances involved in insulin-related hypoglycemia and errors (IHEs) can inform approaches to individualizing glycemic targets.

Objective—Describe U.S. burden, rates, and characteristics of emergency department (ED) visits and emergent hospitalizations for IHEs.

Design—Nationally-representative, public health surveillance of adverse drug events and a national, household survey of insulin use.

Setting—National Electronic Injury Surveillance System—Cooperative Adverse Drug Event Surveillance (NEISS-CADES), 2007–2011 and National Health Interview Survey (NHIS), 2007–2011.

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Participants—Insulin-treated patients seeking ED care.

Main outcome(s) and Measures—Estimated annual numbers and estimated annual rates of ED visits and hospitalizations for IHEs among insulin-treated patients with diabetes.

Results—Based on 8,100 cases, an estimated 97,648 (95% confidence interval [CI], 64,410–130,887) ED visits for IHEs occurred annually; almost one-third (29.3% [CI, 21.8%–36.8%]) resulted in hospitalization. Severe neurologic sequelae were documented in an estimated 60.6% (CI, 51.3%–69.9%) of ED visits for IHEs, and glycemic levels ≤50 mg/dL were recorded in over one-half of cases (53.4%). Insulin-treated patients aged ≥80 years were more than twice as likely to visit the ED (rate ratio, 2.5; CI, 1.5–4.3) and nearly five times as likely to be subsequently hospitalized (rate ratio, 4.9; CI, 2.6–9.1) for IHEs than those aged 45–64 years. The most commonly-identified IHE precipitants were reduced food intake and administration of the wrong insulin product.

Conclusions and Relevance—Rates of ED visits and subsequent hospitalizations for IHEs were highest in patients aged ≥80 years; the risks of hypoglycemic sequelae in this age group should be considered in decisions to prescribe and intensify insulin. Meal-planning and insulin product mix-up misadventures are important targets for hypoglycemia prevention efforts.

Insulin is a cornerstone of Type 1 diabetes mellitus (T1DM) treatment and is increasingly introduced early in the treatment course for patients with Type 2 DM (T2DM), who account for 90% to 95% of new DM cases annually.[1] Over the last decade, the number of U.S. patients with insulin-treated DM rose 50%; one-third of patients with diabetes currently use insulin,[2] and in 2012, insulin was estimated to cost the U.S. healthcare system approximately $6 billion.[3] Tight glycemic control with insulin has been associated with reductions in disease complications among patients with T1DM,[4] but has been increasingly associated with harms among patients with T2DM.[5–7] Insulin remains one of the most challenging and limiting aspects of DM medical management owing to complexities in dosing and administration, as well as need for routine monitoring of blood glucose (BG) and food intake to avoid potentially fatal hypoglycemia.[8] The risk of insulin-related hypoglycemia is an important consideration when choosing among treatment options and individualizing glycemic targets, particularly in patients for whom benefits of intensive control may not be as likely realized.[9, 10]

We used recent, nationally-representative data to estimate the burden and rates of insulinrelated hypoglycemia and errors (IHEs) resulting in emergency department (ED) visits and subsequent hospitalizations, and identify high-risk groups and precipitating factors for IHEs.

METHODS

DATA SOURCES & COLLECTION METHODS

Numerator Data—We estimated the numbers of U.S. ED visits and hospitalizations for IHEs based on data from the 63 hospitals participating in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project, a stable, nationally-representative, size-stratified probability sample of hospitals

(excluding psychiatric and penal institutions) in the U.S. and its territories with a minimum of 6 beds and a 24-hour emergency department (Figure 1).[11] As described elsewhere,[12] trained coders at each hospital review clinical records of every ED visit to identify physician-diagnosed adverse drug events (ADEs), and report up to two medications implicated in the adverse event as well as any concomitant medications documented in the medical record. Coders also record narrative descriptions of the ADE, including preceding events, physician diagnosis, clinical and laboratory testing, treatment administered by emergency medical services (EMS) or ED staff, and discharge disposition.

Denominator Data—We estimated the numbers of U.S. patients who reported having DM and using insulin or oral diabetes agents from the National Health Interview Survey (NHIS), a multistage cluster sample of non-institutionalized civilian households (Figure 1).[13]

Institutional Review Board Approval—NEISS-CADES data collection is considered a public health surveillance activity by federal human subjects oversight bodies and does not require human subject review or institutional review board (IRB) approval.[14] NHIS data collection is approved by the IRB at the National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD. No approval is necessary for analyses of deidentified survey data.[15]

DEFINITIONS

ED visits for IHEs included visits to any NEISS-CADES ED from January 1, 2007 through December 31, 2011 in which there was clinician documentation of (1) insulin-related clinically relevant hypoglycemia (BG <70 mg/dL, diagnosis of “hypoglycemia”, or treatment for hypoglycemia), or (2) “insulin overdose” or “insulin reaction”, or (3) an error in insulin use (e.g., administration of the wrong insulin dose). ED visits for allergic reactions, local effects (e.g., injection site pain), non-hypoglycemic effects (e.g., “headache” alone) and accidental needlesticks were excluded. Definitions of other variables, including IHE location, clinical presentation, BG levels, hypoglycemia treatments, diabetes therapy, and precipitating factors are provided in eTable 1.

Prevalence of self-reported diabetes from January 1, 2007 through December 31, 2011 was estimated from the number of NHIS respondents who answered “Yes” to the question, “Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?”.[16–18] For those ≥ 18 years of age, prevalence of insulin-treated diabetes was estimated via the number of NHIS respondents who answered “Yes” to the question, “Are you now taking insulin?”. For those <18 years of age, this question is not asked; thus, prevalence of diagnosed diabetes was used as a proxy for insulin treatment. Insulin-treated patients were considered to be treated with both insulin and oral diabetes agent(s) if they also answered “Yes” to the question, “Are you now taking diabetic pills to lower your blood sugar?”.

STATISTICAL ANALYSIS

Each NEISS-CADES record is accompanied by a sample weight based on inverse probability of selection, adjusted for non-response and hospital non-participation, and post-

stratified to account for changes in the number of U.S. ED visits each year. Each NHIS record is accompanied by a sample weight based on non-zero probability of selection, with design, ratio, non-response and post-stratification adjustments; post-stratification adjustment is made relative to census control totals for the number of U.S. civilian, non-institutionalized individuals.[19]

National estimates and proportions of ED visits and hospitalizations for IHEs and national estimates of patients with diabetes using insulin alone or in combination with oral diabetes agents, with corresponding 95% confidence intervals (CIs) were calculated using the SURVEYMEANS procedure in SAS (version 9.3, SAS Institute, Cary, NC) to account for the sample weights and complex sample designs. Estimates and their corresponding CIs derived from 2007–2011 NEISS-CADES and NHIS data were divided by 5 to obtain average annual estimates and CIs. Estimates based on small numbers of cases (<20) or with a coefficient of variation greater than 30% were considered statistically unstable and are noted in the tables. National estimates were calculated for variables with completed documentation (≥90% of cases); case-based analysis was used for remaining variables.

To estimate rates of ED visits and hospitalizations for IHEs in relation to insulin exposure, we divided (NEISS-CADES-derived) estimates of ED visits or hospitalizations for IHEs by (NHIS-derived) estimates of insulin-treated patients. A similar approach was used to estimate the rates of IHEs by age and sex. Accompanying CIs were calculated accounting for variability in both numerator and denominator estimates, and assuming statistical independence (as these components were derived from separate surveys).[20] These rate estimates were then used to calculate rate ratios (RRs) of ED visits and hospitalizations for IHEs associated with different patient groups. Estimated CIs for RRs were calculated using an initial logarithmic transformation and incorporated the estimated variances of the numerators and denominators of both component rate estimates, which were assumed to be independent across patient populations.[21]

RESULTS

NUMBERS OF ED VISITS

Based on 8,100 NEISS-CADES surveillance cases, an estimated 97,648 (CI, 64,410–130,887) ED visits for IHEs occurred annually between 2007 and 2011 (Table 1), accounting for 9.2% (CI, 6.7%–11.8%) of ED visits for all ADEs during this period. Among the very elderly (≥80 years of age), ED visits for IHEs accounted for 12.4% (CI, 8.9%–16.0%) of ED visits for all ADEs. The estimated median age of patients who presented to EDs for IHEs was 60 years for patients treated with insulin alone and 67 years for patients treated with insulin and at least one oral diabetes agent. An estimated 50.4% (CI, 46.4%–54.3%) of ED visits for IHEs occurred among males. Among adults (≥18 years of age), at least one oral diabetes agent was documented in addition to insulin in an estimated 17.1% (CI, 13.3%–20.8%) of ED visits for IHEs (Table 2).

RATES OF ED VISITS AND HOSPITALIZATIONS

Patients ≥80 years of age had the highest estimated rate of ED visits for IHEs (34.9 per 1,000 insulin-treated patients with diabetes; CI, 20.5–49.3), followed by patients 18–44 years of age (24.3 per 1,000; CI, 15.0–33.6). When all patients ≥65 years of age are considered, the estimated rate was 20.5 per 1000 (CI, 13.2–27.8). Insulin-treated patients ≥80 years of age were more than twice as likely to seek ED evaluation for IHEs than those 65–79 years of age (RR, 2.1; CI, 1.3–3.7) and those 45–64 years of age (RR, 2.5; CI, 1.5–4.3) (Table 2). Patients ≥80 years of age were also almost five times as likely to be hospitalized for IHEs than those 45–64 years of age (RR, 4.9; CI, 2.6.–9.1). No significant differences in the rates of ED visits (RR, 1.0; CI, 0.6–1.6) or hospitalizations (RR, 1.2; CI, 0.6–2.1) for IHEs were identified between female and male patients. Overall, the rate of ED visits for IHEs among patients ≥18 years of age treated with insulin only was five times that of patients treated with insulin and at least one oral diabetes agent (RR, 5.3; CI, 3.2–8.8); the RR decreased as patient age increased (Table 2).

SPECIFIC INSULIN AND CONCOMITANT ORAL AGENTS

In an estimated 22.9% of ED visits for IHEs, more than one type of insulin product was documented in the medical record (Table 3). Long-acting (32.9%) and rapid-acting (26.4%) products were the most commonly-documented insulin product types (eTable 2). Metformin and sulfonylureas were the most commonly-documented concomitant oral diabetes agents, identified in 50.9% (CI, 47.6%–54.2%) and 39.2% (CI, 34.8%–43.6%) of estimated ED visits for IHEs where an oral diabetes agent was documented, respectively.

IHE CHARACTERISTICS – NATIONAL ESTIMATES

Hypoglycemia was documented in an estimated 95.4% of ED visits for IHEs, and severe neurologic sequelae (i.e., hypoglycemia-associated shock, loss of consciousness, or seizure; hypoglycemia-associated injury or fall; or hypoglycemia-associated altered mental status) were documented in an estimated 60.6% (CI, 51.3%–69.9%) of ED visits (Table 3). Almost one-third (29.3%) of estimated ED visits for IHEs required admission, transfer to another facility, or observation admission; observation admissions comprised 2.1% (CI, 0.9%–3.3%) of estimated ED visits.

IHE CHARACTERISTICS – CASE-BASED ANALYSIS

In most cases (53.3%), IHEs occurred in a home setting (eTable 2). Use of an insulin pump was documented in 6.1% of cases. Over one-half (53.4%) of cases involved a BG level ≤50 mg/dL. Intravenous dextrose 50% was the most common EMS/ED treatment administered (50.8% of cases).

PRECIPITATING FACTORS

Precipitating factors for ED visits for IHEs were documented in an estimated 20.8% (CI, 14.8%–26.9%) of ED visits. When documented, almost one-half (45.9%) involved meal-related misadventures (e.g., neglecting to eat shortly after taking a rapid-acting insulin, not adjusting insulin regimen in the presence of reduced caloric intake) (Table 4). Taking the wrong insulin product was documented in an estimated 22.1% of ED visits for IHEs with

documented precipitants, and taking the wrong dose or confusing dosing units was documented in an estimated 12.2% of ED visits with documented precipitants. Among ED visits for IHEs where taking the wrong insulin was documented, the most commonly reported error was mixing up long-acting and rapid-acting insulin products. In an estimated 52.3% (CI, 42.5%–62.0%) of these ED visits, patients reported an intent to take a long-acting insulin product (e.g., detemir, glargine), but took a rapid-acting one (e.g., aspart, lispro) instead. The proportion hospitalized did not differ among ED visits where an IHE precipitant was documented (20.7%; CI, 15.9%–25.4%) compared with ED visits without an IHE precipitant documented (31.6%; CI, 22.9%–40.2%).

DISCUSSION

Insulin is an important component of diabetes treatment, but remains complex to manage and poses serious risk of hypoglycemia.[22] These national data quantify the burden and severity of IHEs, identify patient groups at higher risk for these events, and describe precipitating factors that could be targeted by prevention efforts.

Nearly 100,000 ED visits and 30,000 hospitalizations annually for IHEs demonstrate the high frequency and significant health impact of these adverse events. Based on prior cost estimates of ED visits for hypoglycemia,[23] ED visits for IHEs may have cost well over $600 million during the 5-year study period. Direct comparisons of our findings to those of previous studies are limited by differences in study methodologies. One study estimated 40,700 ED visits for insulin and other diabetes agent-related adverse events in 2010 using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes for poisoning (962.3) or adverse effects due to insulin or other diabetes agents (E932.3);[24] however, cause-of-injury codes such as these have low sensitivity for identifying many ADEs.[25] Another study estimated that 316,000 visits for hypoglycemia were made to U.S. EDs in 2007 based on reporting of hypoglycemia as the first-listed diagnosis and diabetes as a secondary diagnosis;[26] however, this analysis lacked information on insulin use and could not exclude hypoglycemia episodes related to other factors (e.g., alcohol use, occult infection).

The IHEs we identified were serious events, with BG levels ≤50 mg/dL in over half of cases and severe neurologic manifestations in almost two-thirds of cases. We have previously found insulin to be one of the most commonly implicated drugs in adverse events treated in EDs.[27] Based on the more recent data in this study, IHEs accounted for 1 out of every 8 estimated ED visits for ADEs among the very elderly (≥80 years of age), who sought ED evaluation and were hospitalized for IHEs at rates two and five times higher than those 45–64 years of age, respectively. Other studies have found that Medicare beneficiaries ≥85 years of age are twice as likely to experience a hypoglycemia-related hospitalization compared with those 65–74 years of age,[28] and that re-hospitalizations and mortality are more frequent among older adults (≥66 years of age) with at least one episode of hospitalized hypoglycemia.[29]

Although there are notable exceptions,[30–33] until very recently, most diabetes treatment guidelines, quality metrics, and pay-for-performance measures placed little emphasis on

hypoglycemia risk factors such as advanced age, limited life expectancy, or frailty.[34] The higher rates of ED visits and hospitalizations for IHEs among older insulin-treated patients with diabetes suggest that individualizing glycemic targets by balancing hypoglycemia risks with long-term benefits of glycemic control is appropriate.[22, 35–37] Updated guidelines and treatment recommendations are now advising glycemic targets be relaxed for patients with advanced age, high risk of hypoglycemia or shorter life expectancy.[22, 35, 38, 39] For example, the American Geriatrics Society has advocated for avoiding adding medications to achieve tight hemoglobin A_{1c} control in most adults ≥65 years of age.[40, 41] Tighter glycemic control may continue to be appropriate for functional and cognitively intact elderly patients with diabetes who have longer life expectancy and for whom intensive insulin therapy can be managed safely;[22, 35] however, the high frequency and severity of ED visits for IHEs suggest careful consideration of hypoglycemic sequelae and a cautious approach when deciding whether to start or intensify insulin treatment among older adults, especially the very elderly.

Adoption of a patient-centered approach to setting glycemic targets[9, 10, 42–44] also requires development of healthcare quality metrics which recognize targets based on individual patients' clinical profiles and preferences.[33] Although current National Quality Forum-endorsed quality metrics do not yet incorporate variation in A_{1c} target levels based on hypoglycemia risk,[45, 46] new quality measures might allow for considerations of hypoglycemia risks along with long-term benefits of glycemic control.[47]

Enhanced prevention efforts should target commonly-identified IHE precipitants.[48] Although meal-planning is a well-recognized component of diabetes self-management education,[49, 50] the most commonly-documented IHE precipitant in this study was meal-related misadventure, suggesting further emphasis on meal-planning in diabetes patient education efforts may be needed. Reducing the frequency of missed meals and improving patients' competency in adjusting insulin regimens when food intake is reduced may require both content review (e.g., reviewing patients' understanding of dietetic needs in relation to BG levels) and simulation (e.g., patients demonstrating how they would manage insulin with a missed meal or reduced food intake scenario).[48, 51]

Administration of the wrong insulin product (e.g., rapid-acting vs. long-acting agents) was the second most commonly-documented IHE precipitant. The number of U.S. poison control center calls for insulin-related unintentional therapeutic errors increased in the last decade, but the frequency of specific errors, such as using the wrong insulin product, has not been described.[52, 53] Recently, insulin packaging has become more distinguishable;[54] however, mix-ups continue[55] and further product type distinctions (e.g., using packaging color or texture) might be explored for reducing medication errors. Also, diabetes self-management education might emphasize distinguishing insulin types, minimizing mix-ups (e.g., storing rapid-acting and long-acting agents in different locations), and correctly timing insulin administration.[54, 56]

This study's findings should be interpreted in the context of the limitations of public health surveillance data. First, these data likely underestimate the total burden of hypoglycemic events as hypoglycemia, although a frequent cause of EMS calls,[57–61] is most often cared

for outside of the ED setting.[62] Patients who have hypoglycemia unawareness[63, 64] and whose episodes may not result in EMS or ED care are not counted. Patients who died en route to or in the ED are also not counted. Second, since information on past medical history is limited in the ED medical record, the contributions of risk factors for hypoglycemia such as DM type, intensity and duration of insulin therapy, glycemic control, concomitant medications, and comorbidities were not assessed. Third, the specific insulin brand, formulation, and delivery system were not always documented, which limited the ability to assess differences in ED visits and hospitalizations for IHEs across specific insulin products. Similarly, we did not make detailed comparisons between patients treated with insulin alone and those treated with insulin and oral diabetes agent(s) because documentation of concurrent oral diabetes therapy may have been incomplete. Nonetheless, it is notable that across all adult age groups the rate of estimated ED visits for IHEs was consistently lower among those treated with concurrent oral diabetes therapy, perhaps suggesting concurrent use of long-acting insulin products, with less risk for hypoglycemia.[65] Fourth, BG levels were not specified in approximately one-third of cases; nevertheless, over half of cases still had documented BG ≤50 mg/dL. Other indicators of the seriousness of these events included almost 60,000 estimated ED visits for IHEs with severe neurologic sequelae and almost 30,000 estimated ED visits resulting in hospitalization.

Insulin-related hypoglycemia and errors are clinically significant causes of ED visits and hospitalizations for ADEs, particularly among very elderly patients with diabetes. Reducing ED visits for adverse events related to injectable diabetes agents has been recognized as a national priority for improving the health of Americans in a new Healthy People 2020 goal.[66] Reaching this goal will likely require balancing glycemic risks in vulnerable older patient populations and augmenting prevention efforts targeted at key IHE precipitants, such as meal-related misadventures and insulin product mix-ups. Healthcare quality metrics should evolve based on the most current glycemic control guidelines, and the impact of changing guidelines, quality metrics, and prevention strategies should be evaluated via ongoing national surveillance.[22, 35, 67–69]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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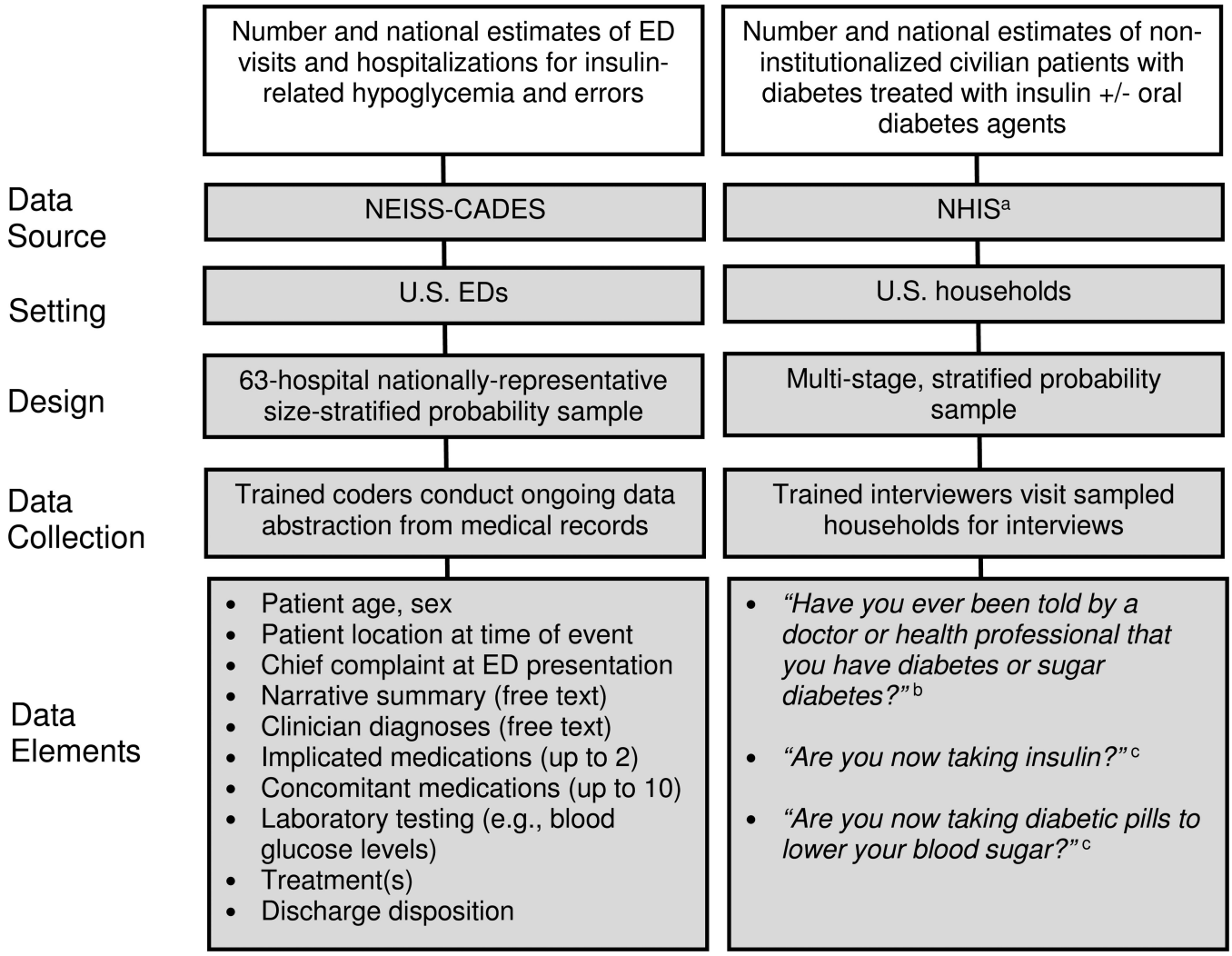

Abbreviations: ED, emergency department; EMS, emergency medical services; NEISS-CADES, National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance;[11, 12] NHIS, National Health Interview Survey.[13]
[a] NHIS Core Questionnaire (Sample Adult and Sample Child components).
[b] Responses from persons who answered they had "borderline" diabetes are treated as unknown. For female respondents, this question begins with the phrase, "Other than during pregnancy".
[c] For persons <18 years of age, these questions are not asked; for this age group, prevalence of diagnosed diabetes was used as a proxy for national estimates of insulin treatment.

Figure 1.

Data sources and Descriptions.

Abbreviations: ED, emergency department; EMS, emergency medical services; NEISS-CADES, National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance;[11, 12] NHIS, National Health Interview Survey.[13]
[a] NHIS Core Questionnaire (Sample Adult and Sample Child components).
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Table 1

Number of Cases and Estimates of Emergency Department Visits for Insulin-related Hypoglycemia and Errors, by Patient Characteristics—United States, 2007–2011[a]

Patient Characteristics	ED Visits for IHEs			Persons with Diabetes Mellitus Treated with Insulin +/− Oral Diabetes Agents		ED Visits Per 1,000 Persons with Diabetes Mellitus Treated with Insulin +/− Oral Diabetes Agents	
	Cases	Annual National Estimate		Annual National Estimate		Annual National Estimate	95% Confidence Interval
	No.	No.	%	No.	%		
Age							
<18 years[b]	265	2,088	2.1	152,555	2.8	13.7	4.9 – 22.5
18–44 years	1,675	21,189	21.7	871,150	15.9	24.3	15.0 – 33.6
45–64 years	2,817	34,173	35.0	2,492,704	45.5	13.7	9.1 – 18.3
65–79 years	2,190	24,720	25.3	1,515,077	27.7	16.3	10.7 – 21.9
≥80 years	1,153	15,479	15.9	443,497	8.1	34.9	20.5 – 49.3
Sex[c]							
Female	4,080	48,458	49.6	2,740,352	50.1	17.7	11.9 – 23.5
Male	4,019	49,186	50.4	2,734,631	49.9	18.0	11.4 – 24.5
Total	**8,100**	**97,648**	~	~	~	~	~

Abbreviations: ED, emergency department; IHEs, insulin-related hypoglycemia and errors.

[a] Case counts and estimates from the National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project, CDC. Diabetes prevalence estimates from the National Health Interview Survey (NHIS), CDC.

[b] For persons <18 years of age, diabetes therapy is not reported by NHIS; for this age group, prevalence of diagnosed diabetes was used as a proxy for national estimates of insulin treatment.

[c] Sex missing for one case.

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Table 2

Number of Cases and Estimates of Emergency Department Visits for Insulin-related Hypoglycemia and Errors, by Diabetes Therapy and Patient Age—United States, 2007–2011[a]

Diabetes Therapy by Patient Age	ED Visits for IHEs			Persons with Diabetes Mellitus Treated with Insulin +/− Oral Diabetes Agents		ED Visits Per 1,000 Persons with Diabetes Mellitus Treated with Insulin +/− Oral Diabetes Agents	
	Cases	Annual National Estimate		Annual National Estimate		Annual National Estimate	95% Confidence Interval
	No.	No.	%	No.	%		
<18 years[b]							
Insulin only	261	2,051	98.2	n/a	n/a	n/a	n/a
Insulin + oral agent	4	*c*	*c*	n/a	n/a	n/a	n/a
≥18 years							
Insulin only	6,492	79,245	82.9	2,553,062	48	31.0	20.3 – 41.7
Insulin + oral agent	1,343	16,315	17.1	2,769,366	52	5.9	3.7 – 8.1
18–44 years							
Insulin only	1,580	20,190	95.3	579,860	66.6	34.8	21.1 – 48.5
Insulin + oral agent	95	999	4.7	291,290	33.4	3.4	1.8 – 5.1
45–64 years							
Insulin only	2,322	28,029	82.0	1,042,828	41.8	26.9	17.3 – 36.5
Insulin + oral agent	495	6,144	18.0	1,449,876	58.2	4.2	2.5 – 6.0
65–79 years							
Insulin only	1,672	18,836	76.2	688,371	45.4	27.4	17.5 – 37.2
Insulin + oral agent	518	5,884	23.8	826,706	54.6	7.1	4.2 – 10.0
≥80 years							
Insulin only	918	12,190	78.8	242,003	54.6	50.4	28.6 – 72.1
Insulin + oral agent	235	3,289	21.2	201,493	45.4	16.3	8.0 – 24.7
Total	**8,100**	**97,648**	~	~	~	~	~

Abbreviations: ED, emergency department; IHEs, insulin-related hypoglycemia and errors; n/a, not applicable.

[a] Case counts and estimates from the National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project, CDC. Diabetes prevalence estimates from the National Health Interview Survey (NHIS), CDC. "Insulin only" refers to cases where only insulin was documented in the ED medical record and no concomitant oral diabetes agent was documented. "Insulin + oral agent" refers to cases where an oral diabetes agent was documented in addition to insulin in the ED medical record.

[b] For persons <18 years of age, diabetes therapy is not reported by NHIS; treatment-specific rates were not calculated for this age group ("n/a").

[c] Estimates based on fewer than 20 cases are not shown.

Table 3

Number of Cases and Estimates of Emergency Department Visits for Insulin-related Hypoglycemia and Errors, by Case Characteristics—United States, 2007–2011[a]

Case Characteristics	ED Visits for IHEs		
	Cases	Annual National Estimate	
	No.	%	95% Confidence Interval
Number of Insulin Products[b]			
1	6,149	77.1	71.3 – 83.0
2	1,892	22.3	16.5 – 28.0
≥3	59	0.6	0.3 – 0.9
Other Diabetes Agents[c]			
Biguanide (metformin)	705	8.5	6.7 – 10.4
Sulfonylurea	500	6.6	4.7 – 8.5
Thiazolidinedione (glitazones)	312	3.6	2.4 – 4.7
Dipeptidyl peptidase-4 inhibitor (gliptins)	82	1.3	0.6 – 2.0
Other / unspecified oral agent	73	0.9	0.5 – 1.4
Exenatide, liraglutide, pramlintide	21	0.2	0.1 – 0.4
Clinical Presentation of Event			
Hypoglycemia	7,760	95.4	93.6 – 97.2
With shock, loss of consciousness, or seizure	1,846	23.2	15.5 – 31.0
With fall or injury	491	5.1	3.7 – 6.4
With altered mental status	2,535	32.3	20.6 – 44.0
With other neurologic sequelae	416	4.8	3.3 – 6.3
With presyncope/syncope	398	4.4	3.3 – 5.6
With other sequelae	439	5.6	3.8 – 7.4
Without specific sequelae documented	1,635	20.0	13.4 – 26.6
No hypoglycemia documented[d]	340	4.6	2.8 – 6.4
Discharge Disposition[e]			
Admitted, transferred, or held for observation	2,447	29.3	21.8 – 36.8
Treated and released, or left against medical advice	5,652	70.7	63.2 – 78.2

Abbreviations: ED, emergency department; IHEs, insulin-related hypoglycemia and errors.

[a] Case counts and estimates from the National Electronic Injury Surveillance System - Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project, CDC. Refer to eTable 1 for definitions of case characteristics.

[b] All insulin products reported in the ED medical record, including those implicated in IHEs and those listed as concomitant medications.

[c] Categories are not mutually exclusive; therefore, percentages may total more than 100%.

[d] Clinician documentation of error in insulin use (n=323), “insulin overdose” (n=6), or “insulin reaction” (n=11) with no documentation of hypoglycemia.

[e] Discharge disposition missing for one case.

Table 4

Number of Cases and Estimates of Precipitating Factors Identified in Emergency Department Visits for Insulin-related Hypoglycemia and Errors—United States, 2007–2011[a]

Precipitating Factors	ED Visits for IHEs			Illustrative Cases[b]
	Cases, No.	Annual National Estimate		
		%	95% Confidence Interval	
Meal-related misadventure	952	45.9	38.2 – 53.6	• Unrestrained 19 YOF driver hit tree & brick wall. Blood sugar was 24. Took insulin 2 hours ago, but no time to eat. Diagnosis: Scalp abrasion, hypoglycemia. • 75 YOM is an insulin-dependent diabetic, had a syncopal episode at home, found with blood sugar in the 20's by paramedics. EMS gave patient an amp of D50 IV. Per wife, patient has been having low blood sugar & it has been difficult to keep elevated. She feels it is due to chemo, possibly not eating enough. Diagnosis: Hypoglycemia.
Unintentionally took wrong insulin product	332	22.1	17.2 – 26.9	• 51 YOM, per spouse she injected patient with 50 units of NovoLog instead of 50 units of Lantus, blood glucose 33 at time of arrival. Diagnosis: Hypoglycemia. • 67 YOM accidentally took wrong medication. Confused Humalog insulin with Humulin insulin, blood sugar 36. Diagnosis: Hypoglycemia.
Unintentionally took wrong dose / Confused units	205	12.2	9.2 – 15.2	• Patient started new insulin regimen, 30–35 units of Lantus, 3–6 units of NovoLog, patient took 35 units of NovoLog accidentally, Blood sugar 40. Diagnosis: Insulin OD. • 62 YOM given 40 units of regular insulin instead of 4, fingerstick blood sugar 47. Diagnosis: insulin overdose, hypoglycemia.
Intentionally took "additional" dose	113	6.0	4.4 – 7.6	• 69 YOM hypoglycemic--patient's blood sugar was over 400; took 12 units insulin in addition to his insulin pump--Blood sugar dropped to 38; found unresponsive by wife. Diagnosis: Insulin shock.
Pump-related misadventure	38	1.5	0.7 – 2.2	• 33 YOF accidentally gave self bolus of 36 units regular insulin while changing insulin pump. Diagnosis: Overdose, accidental. • 27 YOM is an insulin-dependent diabetic on insulin pump, had a witnessed tonoclonic seizure, EMS found blood sugar of 20. Patient admitted that he had eaten dinner but his pump had run out so he gave himself an injection & feels he may have overcompensated. Diagnosis: Hypoglycemia, seizure.
Other misadventure[c]	211	13.4	10.4 – 16.4	• 76 YOM with syncopal episode after mowing lawn for 3 hours; took usual insulin at noon rather than AM--passed out. Diagnosis: Hypoglycemic reaction.

Abbreviations: ED, emergency department; EMS, emergency medical services; IHEs, insulin-related hypoglycemia and errors.

[a] Case counts and estimates from the National Electronic Injury Surveillance System - Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project, CDC. Percentages are out of a total of 1,829 cases (20,346 estimated ED visits) where a precipitating factor was documented. Refer to eTable 1 for definitions of precipitating factors. Categories are not mutually exclusive; therefore, percentages may total more than 100%.

[b] Case descriptions are verbatim excerpts as reported by medical coders based on review of ED medical record narrative (with spelling corrected and abbreviations spelled out).

[c] "Other misadventure" includes: insulin administration at the incorrect time or without regard to checking blood glucose, administration of "too much insulin" not further described, or medication error with insulin not otherwise specified.